REMARKS

Claims 1-20 are pending in the subject application. By this Amendment, applicants have canceled claims 2, 3, 12 and 13 without prejudice or disclaimer and have amended claims 1 and 11. The amendment places the application in condition for allowance or in better form for appeal. Upon entry of this Amendment, claims 1, 4-11, and 14-20 as amended will be pending and under examination.

Applicants maintain that the amendments to claims 1 and 11 do not raise an issue of new matter. Support for the amendments to claims 1 and 11 can be found *inter alia* in the specification on at least page 3, line 34 through page 4, line 9; page 4, lines 22-29; page 7, lines 28-30; and page 41, line 26 through page 43, line 13.

Accordingly, applicants respectfully request that the Amendment be entered.

Rejections under 35 U.S.C. §112, First Paragraph

Claims 1-20 stand rejected under the written description requirement of 35 U.S.C. §112, first paragraph, for the full breadth of the claims. The Examiner stated that a method for determining whether a subject has endometrial cancer comprising assaying for GLUTx expression meets the written description provision of 35 U.S.C. §112, first paragraph. However, the Examiner maintained that the application does not describe that GLUTx expression is upregulated in breast cancer.

Applicants have amended independent claims 1 and 11 to recite that "the defect in cell proliferation is a mammary adenocarcinoma or an endometrial adenocarcinoma..."

Applicants note that on page 2, lines 13-14, the specification describes that "GLUTx is overexpressed in tumors..." In referring to immunoblot analysis of GLUTx in mouse mammary tumors, it is stated on page 3, lines 28-30 that "The GLUTx was induced by the overexpression of oncogenes neu, myc, and ras, that were driven by the

mouse mammary tumor (MMTV) promoter." [Emphasis added.] In addition, the results presented on page 3, line 36 through page 4, line 8, indicate that GLUTx is 3-fold more abundant in metastatic mammary adenocarcinoma MTLn3 cells than in non-metastatic mammary adenocarcinoma MTC cells. Furthermore, as indicated in the first paragraph of the specification, this application is a continuation-in-part of U.S. Patent Application No. 09/516,493, filed March 1, 2000, the entire contents of which are expressly incorporated by reference. Applicants attach hereto pages 38-40 from U.S. Patent Application No. 09/516,493, which includes "Example 10." On page 39, first paragraph, particularly lines 8-11, the specification describes that using Western blot analysis, mouse mammary tumor showed GLUTx protein band while normal mouse mammary tissue did not.

In view of the amendments and remarks made hereinabove, reconsideration and withdrawal of this ground of rejection are respectfully requested.

Rejections under 35 U.S.C. §102(e)

Claims 1-20 stand rejected under 35 U.S.C. §102(e) as anticipated by Baughn et al. (U.S. Patent Application Publication No. US 2003/0171275 A1, December 20, 2000).

Applicants respectfully traverse this rejection.

Applicants note that:

> A rejection for anticipation under section 102 requires that each and every limitation of the claimed invention be disclosed in a single prior art reference. *In re Spada*, 911 F.2d 705, 708, 15 USPQ2d 1655, 1657 (Fed.Cir.1990). In addition, the reference must be enabling and describe the applicant's claimed invention sufficiently to have placed it in possession of a person of ordinary skill in the field of the invention. *Id.* *In re Paulsen*, 30 F.3d 1475, 1478-1479, 31 USPQ 2d 1671, 1673 (Fed. Cir.1994).

Baughn et al. do not disclose that expression of a polypeptide having the sequence set forth in SEQ ID NO:1 is elevated above normal when a subject has a mammary adenocarcinoma or an endometrial adenocarcinoma, as required by the inventions claimed in claims 1 and 11.

Accordingly, Baughn et al. do not anticipate the claimed invention, and applicants respectfully request reconsideration and withdrawal of this ground of rejection.

CONCLUSIONS

In view of the amendments and remarks made hereinabove, applicants respectfully request that the Examiner reconsider and withdraw the rejections in the June 16, 2004 Final Office Action and earnestly solicit allowance of the claims under examination, namely claims 1, 4-11, and 14-20.

If there are any minor matters that prevent allowance of the subject application, applicants request that the Examiner telephone the attorneys indicated below.

No fee is deemed necessary in connection with the filing of this response. However, if any fee is required to preserve the pending of the subject application, authorization is hereby given to charge any such fee to Deposit Account No. 01-1785.

Respectfully submitted,

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increased coupling of the electron transport chain and oxidative phosphorylation in order to maintain high energy phosphate stores. Muscular mitochondrial hypertrophy is noted with endurance training (Holloszy, J.O. and Booth, F.W., *Annu Rev Physiol* 38: 273-291, 1976). Interestingly, mitochondrial hypertrophy is also noted in yeast which have been starved for glucose (Lin, et al., *Arch Biochem Biophys* 160: 458-464, 1974; Mian, et al., *J Bacteriol* 115: 876-881, 1973). The commonality of metabolic stress is noted with endurance training and glucose starvation, therefore, GLUT4 null muscle may be in a similar 'stressed' state which activates or enhances GLUTx expression. All of the above lend further support to the contention that GLUT4 null mice have made metabolic/genetic adaptations similar to those achieved by endurance trained athletes.

The inventors have hypothesized that similar metabolic/genetic alterations are induced by TDZ treatment. Indeed GLUT4 null muscle appears to have activated PPARg as evidenced by ectopic/unpredicted expression of an aP2-GLUT4 transgene in muscle and fat. As the adipocyte specific aP2 gene is activated by the transcription factor PPARg, expression of the adipose-restricted aP2-GLUT4 transgene (provided by Dr. B.B. Kahn; (Shepherd, et al., *J Biol Chem* 268: 22243-22246, 1993) in muscle of GLUT4 null mice was unexpected. Additionally, PPARg is upregulated in adipose tissue of GLUT4 null mice which is further suggestive that GLUT4 null mice have activated PPARg by endogenous mechanisms.

Example 9

Preliminary in situ hybridization studies indicate that GLUTx is expressed in the cerebellum and hippocampus of GLUT4 null mice, the same areas where GLUT 4 is expressed in wild type mice. These studies suggest GLUTx may function as a glucose sensor or receptor in the "obesity center" of the brain, and may therefore provide an attractive target for the study and treatment of obesity.

Example 10

A polyclonal antibody was generated to the last 11 amino acids of the

carboxy-terminus of the GLUTx protein. These amino acids are LEQITAHFEGR. The antibody was used in Western blot analysis of different tissues from GLUT4 null and wild type mice and of mammary tumors induced by the mouse mammary tumor virus. A specific immunoreactive protein was found to be about 32.6 kD in testis, heart, fat, liver, diaphragm, and soleus muscle in both GLUT4 null and wild type mice. Further analysis revealed that GLUTx protein appears to be more abundant in GLUT4 null liver and testis than in the same wild type tissues. In contrast, the GLUT4 null fat seems to express less GLUTx protein than wild type fat. The Western blot analysis of the mouse mammary tumor showed an approximately 32.6 kD protein while normal mouse mammary tissue did not appear to have a band in this area.

Northern blot analysis using a probe to mouse GLUTx shows a band at about 2.4kb. As noted above, the GLUTx mRNA expression varies among tissues of the GLUT4 null and wild type mice and also between GLUT4 null and wild type tissue. In collaboration with Dr. Sylvie Haugel-de Mouzon (INSERM, Paris), a GLUTx probe was used on Northern blots of tissues from normal and streptozoticin diabetic rats and tissue from rats subjected to hyperglycemic clamps to determine the expression of GLUTx mRNA in various metabolic milieu. The mRNA expression of GLUTx was highest in the testis of normal and streptozotocin diabetic rats with brain and placenta expression about one half as much. The liver expresses about one-tenth the amount seen in the testis in the normal rat. GLUTx mRNA expression in testis and brain was the same in normal as in streptozotocin diabetic and hyperglycemic clamp rats, however the livers and placentas of the diabetic and hyperglycemic clamp rats showed a 2 to 3 fold upregulation of GLUTx mRNA expression when compared to normal rats. Streptozotocin is a pancreatic beta cell toxin that induces hyperglycemia and insulinopenia. Since GLUTx mRNA was increased similarly in the streptozotocin treated rats and the rats clamped under hyperglycemic conditions, GLUTx mRNA appears to be regulated by high glucose (and not high insulin). Results of this series of experiments confirm our hyperglycemic clamp results which suggested that GLUTx is glycemia sensitive.

A hydropathy plot was performed on the primary sequence of GLUTx and 12 transmembrane domains identified. All known facilitated GLUTs have 12 transmembrane domains. From this, it can be predicted that the amino terminus of GLUTx may be only approximately 20 amino acids long. In addition to 5' RACE cloning, a mouse BAC clone was isolated that contains the GLUTx genomic sequences. Restriction fragments have been subcloned from the GLUTx BAC and will be sequenced to elucidate the 5' most amino terminal sequences of the GLUTx protein.

All publications mentioned herein above are hereby incorporated by reference in their entirety. While the foregoing invention has been described in some detail for purposes of clarity and understanding, it will be appreciated by one skilled in the art from a reading of the disclosure that various changes in form and detail can be made without departing from the true scope of the invention in the appended claims.